REMARKS

Reconsideration and allowance are respectfully requested.

Claims 26-29 are now pending, with Claim 26 being the sole independent claim.

Claim 26 has been amended. Support in the specification for this amendment is found at least in the paragraph beginning at page 6, lines 17-21. Thus, no new matter has been added.

Claims 1-25 have been cancelled without prejudice to or disclaimer of the subject matter recited therein.

A Second Information Disclosure Statement and a Terminal Disclaimer to Obviate a Double Patenting Rejection Over a "Prior" Patent are filed simultaneously herewith.

Regarding the amendment of the disclosure, it is respectfully submitted that no amendment of the disclosure is warranted, because the material is not relied upon to overcome any objection, rejection, or other requirement imposed by the office. It is further noted that the Clustal method of alignment is well known to those skilled in the art.

Turning now to the Office Action mailed June 20, 2005:

Regarding the Section 112, first paragraph enablement rejection of Claims 26-29, Applicants respectfully traverse.

Applicants submit that the specification enables a person of ordinary skill to make and use the claimed invention commensurate in scope with the pending claims without undue experimentation.

Applicants submit that there is a well-known correlation between brittle-1 activity (i.e., as an adenylate translocator), as disclosed and claimed in the instant specification, and brittle-1 protein structure.

One of ordinary skill in the art would have within his or her knowledge the teachings of Sullivan et al., *Plant Cell* 3:1337-1348 (1991) ("Sullivan"), Palmieri F., *FEBS Lett.* 346:48-54 (1994) ("Palmieri") and Shannon et al., *Plant Physiol.* 117:1235-1252 (1998) ("Shannon"), all cited in the Second Information Disclosure Statement filed simultaneously herewith.

Sullivan discloses the maize brittle-1 protein (SEQ ID NO:21 of the instant specification; NCBI General Identification (GI) No. 231654).

Inspection of the amino terminus reveals a sequence that has characteristics of a plastid transit peptide. See page 1342, column 2.[1] Sullivan proposes the transit peptide-cleavage site to be at amino acid position 75. See page 1341, Figure 5. Sullivan further discloses the protein having sequence similarity to several mitochondrial inner-envelope translocator proteins. See page 1342, column 2. Sullivan also discloses the protein having two putative membrane-spanning domains citing the work of Kyte et al., *J. Mol. Biol.* 157:105-132 (1982) ("Kyte"), cited in the Second Information Disclosure Statement filed simultaneously herewith. See page 1343, column 1.

Palmieri discloses the sequence motif [P-X-(DE)-X-(LIVAT)-(RK)-X-(LRH)-(LIVMFY)], which is also referred to as the "mitochondrial energy signature", is present in mitochondrial carrier proteins in one to three copies at the C-terminal end of the first helix of each repeat. See page 50, column 2.

Shannon discloses the presence of a putative ADP-Glc-binding motif, KTGGL, 40 amino acid residues upstream of the cleavage site proposed by Sullivan for maize brittle-1 protein. Therefore, Shannon proposes an alternative transit-peptide cleavage site 13 amino acids upstream of the putative ADP-Glc-binding motif (amino acid position 24). See page 1247, column 2.

A more recent report in the literature further supports the conclusions of Sullivan and Palmieri. Patron et al., *Plant Physiol.* 135:2088-2097 (2004) ("Patron"), (copy enclosed) discloses the barley ADP-Glc transporter, and its sequence is homologous to the maize ADP-Glc transporter BRITTLE1 (SEQ ID NO:21 of the instant invention).[2] Applicants note that the KTGGL motif

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[1] Applicants note that Sullivan cites two references that discuss chloroplast targeting sequences (Keegstra et al., 1989 and von Heijne et al., 1989).

[2] Patron has a publication date after the earliest filing date of the instant application, Applicants submit that Patron represents the state of knowledge of one of ordinary skill in the art, as of the earliest filing date of the instant application, at least with respect to the plastid transit peptide and membrane spanning domains associated with brittle-1 activity, since these attributes are disclosed in Sullivan, which has a publication date well before the earliest filing date of the instant application.

discussed in Shannon is not present in the barley plastidial ADP-glucose transporter found in Patron (see Appendix A, discussed *infra*). Patron further discloses a search for predicted transmembrane helices (using TMpred; http://www.ch.embnet.org), and suggests there are at least four. See page 2094, column 1. Patron also discloses that helices 1, 3, and 5 contain the conserved motif PX(D/E)XX(K/R) that is predicted to cause the helix to kink. See page 2094, Figure 5.

Appendix A, attached hereto, is a Clustal alignment of the following four protein sequences using the default parameters cited in the specification:

1. SEQ ID NO:18 of the instant claims (wheat brittle-1 protein)
2. SEQ ID NO:21 of the instant specification (maize brittle-1 protein); NCBI GI No. 231654
3. barley plastidial ADP-glucose transporter found in Patron; NCBI GI No. 47156872
4. barley plastidial ADP-glucose transporter; NCBI GI No. 78354955 (on October 31, 2005, this sequence replaced NCBI GI No. 47156872)

The sequence motif [P-X-(DE)-X-(LIVAT)-(RK)-X-(LRH)-(LIVMFY)] and the KTGGL motif discussed above are boxed in Appendix A. The putative transit-peptide cleavage sites, discussed *infra*, are marked with arrows in Appendix A. The amino acids that are identical among all four sequences can be found in Consensus #1.

Appendix B, also attached, is a chart setting forth a comparison of the percent identity (and percent divergence in the lower half triangle), using the Clustal alignment method with the default parameters, between the four protein sequences found in Appendix A.

Appendix C, attached hereto, is the results of a comparison of the hydrophatic profile (for finding transmembrane segments) of SEQ ID NO:18 and SEQ ID NO:21 using the method of Kyte. The software is available at http://bioinformatics.weizmann.ac.il/hydroph/cmp_hydph.html. Applicants note the similarity of the sequences in the C-terminal end.

A search for the predicted transmembrane helices of SEQ ID NO:18 and SEQ ID NO:21 (using TMpred; http://www.ch.embnet.org), suggests there are at least four and five for these sequences, respectively (output not shown).

Moreover, using the well-known ChloroP software, but not limited to, Applicants analyzed the above protein sequences. For more information on ChloroP, see the attached article by Emanuelsson et al., *Protein Science* 8:978-984 (1999), entitled, "ChloroP, a neural network-based method for predicting chloroplast transit peptides and their cleavage sites" (copy enclosed); the software is available at http://www.cbs.dtu.dk/services/ChloroP. The following information was obtained upon analysis:

Name	Length	Score	cTP	CS-score	cTP-length
SEQ ID NO:18 (wheat)	433	0.529	Y	0.595	51
SEQ ID NO:21 (maize)	436	0.526	Y	4.297	44
NCBI GI No. 47156872	396	0.548	Y	1.376	61
NCBI GI No. 78354955	425	0.548	Y	1.376	61

Interpretation of the output is as follows:

Name is the name of the submitted sequence.
Length is the length of the submitted sequence.
Score is the output score from the second step network. The prediction cTP/no cTP is based solely on this score.
cTP tells whether or not this is predicted as a cTP-containing sequence; "Y" means that the sequence is predicted to contain a cTP; "-" means that is predicted not to contain a cTP.
CS-score is the MEME scoring matrix score for the suggested cleavage site.
cTP-length is the predicted length of the presequence.

Applicants note that all four sequences are predicted to contain a chloroplast transit peptide. Patron predicted a plastid transit peptide of 56 amino acids, which they "confirmed" by N-terminal sequencing of the mature protein purified from barley endosperm plastid envelopes. See page 2092, column 2.

Applicants respectfully submit that the specification coupled with the knowledge about brittle-1 protein structure and activity as described *supra*, provides specific guidance to one of ordinary skill as to where amino acid substitutions could be made to result in a polypeptide sequence having 90% sequence identity to SEQ ID NO:18 while still retaining brittle-1 activity. Furthermore, the experimentation necessary to determine activity is not undue in this field. Applicants disclose methods for expressing the recombinant constructs in monocot, dicot and microbial cells (see prophetic Examples 4-6 of the instant specification). With the expressed polypeptide, activity may be determined using routine tests as those described in Shannon (i.e., see page 1, lines 13-16 of the instant specification). Applicants submit that one of ordinary skill in the art could carry out these methods without undue experimentation.

In view of the foregoing, Applicants respectfully request withdrawal of the Section 112, first paragraph enablement rejection of Claims 26-29.

Regarding the Section 112, first paragraph written description rejection of Claims 26-29, Applicants respectfully traverse.

It appears the above-discussion is equally apposite with respect to this ground of rejection. One of ordinary skill in the art would understand that the structure of polypeptide sequences having at least 90% sequence identity to SEQ ID NO:18 would also have brittle-1 activity in view of the foregoing discussion concerning the known correlation of function and structure with respect to brittle-1 activity.

Applicants submit that the specification discloses a representative number of sequences having at least 90% identity to SEQ ID NO:18, and not just SEQ ID NO:2 itself. For example, the specification discloses at page 7, lines 11-14 that, "it is therefore understood that the invention encompasses more than the specific exemplary nucleotide or amino acid sequences and includes functional equivalents thereof." Specific

examples of such substitution are disclosed at least at page 7, line 29 to page 8, line 2.

In view of the foregoing, Applicants respectfully request withdrawal of the Section 112, first paragraph written description rejection of Claims 26-29.

Claims 26-29 are rejected under 35 U.S.C. 112, second paragraph as allegedly indefinite. The amendment to Claim 26 above renders this rejection moot. Applicants respectfully request withdrawal of the 112, second paragraph rejection of Claims 26-29.

Claims 26-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4 of U.S. Patent No. 6,660,850.

Applicants request withdrawal of this rejection in view of the Terminal Disclaimer to Obviate a Double Patenting Rejection Over a "Prior" Patent, which is filed simultaneously herewith.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

Please charge any fees or credit any overpayment of fees which are required in connection with the filing of this Preliminary Amendment and Response to Restriction Requirement to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Allowance of the above-referenced application is respectfully requested in view of the foregoing.

Respectfully submitted,

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Attachements: Appendices A, B and C